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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JAVANMARD, SAHAR	
ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/670,488	JOST-PRICE ET AL.	
	Examiner	Art Unit	
	SAHAR JAVANMARD	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-41,49-53,58,66,70,73,74 and 76* is/are pending in the application.

4a) Of the above claim(s) *22-41,49-53 and 70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21, 58, 66, 73-74 and 76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/4/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/29/2006 has been entered.

Claim(s) 1-41, 49-53, 58, 66, 70, and 73-74 and 76 are pending. Claims 22-41, 49-53 and 70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions. Claim(s) 1-21, 58, 66, 73-74 and 76 are examined herein.

Response to Arguments

In view of Applicant's decision to hold the double patenting rejection of claims 1-21 in abeyance until further notice, the rejection is hereby maintained and is restated below for Applicant's convenience.

In view of Applicant's amendments, the 103(a) rejections of the previous office action (mail date 09/04/09) have been fully considered but are not persuasive. Applicants contend that they have demonstrated unexpected results as evidenced by an affidavit on behalf of Dr. Zimmerman and the submission Exhibit A and Exhibit 1 in response to the previous action. The data is not convincing because in instances where

the alleged synergistic results are very close (i.e., paroxetine (0.375uM) and prednisolone (0.025uM)), there are no ranges for error provided, thus one cannot assume that the necessarily 4.5% difference observed is actually synergy or additivity that is within error. An amendment to the instant claims limiting the claims to the compositions and dosages for which synergistic results truly have been demonstrated, would overcome this rejection.

Thus rejections of the previous office action are hereby maintained and are reiterated below for Applicant's convenience.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887,225 USPQ 645 (Fed. Cir. 1985); *In re Van Omum*, 686 F.2d 937,214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 of copending Application No. 10/947455. Although the conflicting claims are not identical, they are not patentably distinct from each other because

Claim 1 of the present application is drawn to a composition comprising a selective serotonin reuptake inhibitor (SSRI) and a corticosteroid. Claim 2 of the present application further limits the SSRI as being selected from a variety of SSRIs (including paroxetine and fluoxetine). Claim 3 of the present application further limits the corticosteroid as being selected from a variety of corticosteroids (including prednisolone, prednisone and hydrocortisone). Claim 46 of the present application is drawn to a composition comprising an SSRI and a glucocoticoid receptor modulator. Claim 58 of the present application is drawn to a pharmaceutical composition comprising an SSRI and a second compound selected from the group consisting of a xanthine, anticholinergic compound, beta receptor agonist, bronchodialator, NSAID, DMARD, COX-2 inhibitor, non-steroidal calcineurin inhibitor, vitamin D analog, psoralen, retinoid and 5-amino salicylic acid. Claim 73 of the present application is drawn to a kit comprising a composition comprising a SSRI and a corticosteroid and instructions.

Claim 1 of the '455 application is drawn to a composition comprising a SSRI, or analog thereof, and a corticosteroid.

The claims overlap in scope with nearly identical language with exception of the

'455's "analog thereof'.

Claims 1-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24, 51-54, 66-80 and 82-85 of copending Application No. 10/777517. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claim 1 of the present application is drawn to a composition comprising a selective serotonin reuptake inhibitor (SSRI) and a corticosteroid. Claim 2 of the present application further limits the SSRI as being selected from a variety of SSRIs (including paroxetine and fluoxetine). Claim 3 of the present application further limits the corticosteroid as being selected from a variety of corticosteroids (including prednisolone, prednisone and hydrocortisone). Claim 46 of the present application is drawn to a composition comprising an SSRI and a glucocoticoid receptor modulator. Claim 58 of the present application is drawn to a pharmaceutical composition comprising an SSRI and a second compound selected from the group consisting of a xanthine, anticholinergic compound, beta receptor agonist, bronchodialator, NSAID, DMARD, COX-2 inhibitor, n on-steroidal calcineurin inhibitor, vitamin D analog, psoralen, retinoid and 5-amino salicylic acid. Claim 73 of the present application is drawn to a kit comprising a composition comprising a SSRI and a corticosteroid and instructions.

Claim 1 of the '517 application is drawn to a composition comprising a SSRI, or analog thereof, and a corticosteroid.

Claim 2 of the '517 application further limits the SSRI as being selected from a

variety of SSRIs (including paroxetine and fluoxetine). Claim 3 of the '517 application further limits the corticosteroid as being selected from a variety of corticosteroids (including prednisolone, prednisone and hydrocortisone). Claim 51 of the '517 application is drawn to a composition comprising an SSRI and a glucocorticoid receptor 'modulator. Claim 66 of the '517 application is drawn to a pharmaceutical composition comprising an SSRI and a second compound selected from the group consisting of a xanthine, anticholinergic compound, beta receptor agonist, bronchodialator, NSAID, DMARD, COX-2 inhibitor, n on-steroidal calcineurin inhibitor, vitamin D analog, psoralen, retinoid and 5-amino salicylic acid. Claim 82 of the '517 application is drawn to a kit comprising a composition comprising a SSRI or SNRI and a corticosteroid and instructions.

The '517 application differs only in that a SNRI may be utilized as well as a SSRI. The fact that both the '517 and present application utilize open claim language claim 1 of the present application clearly obviates the inclusion of a SNRI compound.

These are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9, 11-12, 15, 19-21, 58, 66, and 73, 74, and 76 rejected under 35 U.S.C. 103(a) as being unpatentable over Siegel et al. (US Patent No. 6204245B1).

Siegel et al. teach, in col. 3 line 49 to col. 4 line 27, "...one treatment regime entails administering at least one immunosuppressive agent selected from the group consisting of a nonsteroidal anti-inflammatory drug, a glucocorticoid, hydroxychloroquine, sulfaxalazine, methotrexate, aurothioglucose, aurothiomalate, auronofin, D-penicillamine, azathioprine, cyclophosphamide, cyclosporin A, FK506, and rapamycin. Another treatment regime entails the administration of at least two of these immunosuppressive agents. A further treatment regime entails administering an immunosuppressive agent in combination with at least one agent selected from the group consisting of a tricyclic antidepressant, a tetracyclic antidepressant, a Selective serotonin reuptake inhibitor (SSRI), a monoamine oxidase (MAO) inhibitor, caffeine,

theophiline, theobromine, amphetamine, methylphenidate, dextroamphetamine, methamphetamine, pemoline, mazindol, modafinil, selegiline, ritanserin, viloxazine, CRL 40476, clomipramine, protriptyline, imipramine, desipramine, fluoxetine, paroxitine, sertraline, gammahydroxybutyrate (GHB), clonazepam, carbamazepine, and yohimbine. In some methods, the glucocorticoid is dexamethasone, methylprednisolone, prednisolone, or prednisone. In some such methods, the glucocorticoid compound is administered in combination with a therapeutically effective amount of a nonsteroidal anti-inflammatory agent. In some such methods, the nonsteroidal anti-inflammatory agent is an aspirin compound (acetylsalicylate), a non-aspirin salicylate, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, meclofenamate, naproxen, naproxen sodium, phenylbutazone, sulindac, or tometin. In some methods, the glucocorticoid compound is administered in combination with a therapeutically effective amount of an agent selected from the group consisting of hydroxychloroquine, sulfaxalazine, methotrexate, aurothioglucose, aurothiomalate, auronofin, D-penicillamine, azathioprine, cyclophosphamide, cyclosporin A, FK506, and rapamycin. In some methods the therapeutic agent is selected from the group consisting of:an anti-inflammatory cytokine, an anti-TNF-V antibody, a COX-1 inhibitor, a COX-2 inhibitor, an iNOS inhibitor, an nNOS inhibitor, and an antioxidant.

The immunosuppressive agent is typically administered by intravenous infusion, transdermal delivery, intramuscular delivery, subcutaneous delivery, intracerebral ventricular delivery, oral delivery, or by inhalation." In col. 10 lines 12-50, Siegel et al. teach suitable treat agents as: "...treatment agents of the present invention include

immunosuppressive agents. Immunosuppressive agents are agents capable of suppressing immune responses. These agents include cytotoxic drugs, corticosteriods, nonsteroidal anti-inflammatory drugs (NSAIDs), specific T-lymphocyte immunosuppressants, and antibodies or fragments thereof (see Physicians' Desk Reference, 53.sup.rd edition, Medical Economics Company Inc., Montvale, N.J. (1999); this reference and all references cited therein are herein incorporated by reference).

Cytotoxic or antimetabolic drugs include hydroxychloroquine, sulfaxalazine, methotrexate, aurothioglucose, aurothiomalate, auronofin,.D-penicillamine, azathioprine, and cyclophosphamide.

Glucocorticoids include dexamethasone, methylprednisolone, prednisolone, and prednisone.

NSAIDs include aspirin compounds (acetylsalicylates), non-aspirin salicylates, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, meclofenamate, naproxen, naproxen sodium, phenylbutazone, sulindac, and tometin.

Specific T-lymphocyte inununosuppressants include cyclosporin A, FK506, and rapamycin.

Treatment agents also can include other agents such as tricyclic antidepressants, tetracyclic antidepressants, SSRIs, monoamine oxidase (MAO) inhibitors, caffeine, theophiline, theobromine, amphetamine, methylphenidate, dextroamphetamine, methamphetamine, pemoline, mazindol, modafinil, selegiline, ritanserin, viloxazine, CRL 40476, clomipramine, protriptyline, imipramine, desipramine,

fluoxetine, paroxitine, sertraline, gammahydroxybutyrate (GHB), clonazepam, carbamazepine, and yohimbine.

Other treatment agents include anti-inflammatory cytokines, anti-TNF-.A-inverted, antibodies, COX-1 inhibitors, COX-2 inhibitors, iNOS inhibitors, nNOS inhibitors, and antioxidants."

In col. 12 line 5 to col. 13 line 11, Siegel et al. teach combination therapies such as: "...therapeutic agents described above can be used alone or in combinations with each other (see, e.g., Aldrich, M., Sleep Medicine, Oxford University Press, New York, N.Y.U.S.A. 1999 and Robinson, A. and Guilleminault, C. "Narcolepsy," in Sleep Disorders Medicine: Basic Science, Technical Considerations, and Clinical Aspects, Chokroverty, S. (ed.) (Butterworh Heinemann Boston, Mass. U.S.A. 1999), pp 427-440; these references and the references cited therein are herein incorporated by reference).

Combination therapy includes administration of a single pharmaceutical dosage formulation which contains an immunosuppressive agent and one or more additional active agents, as well as administration of an immunosuppressive agent and each active agent in its own separate pharmaceutical dosage formulation. For example, a glucocorticoid (e.g., dexamethasone, methylprednisolone, prednisolone, or prednisone) and azathioprine can be administered to the human subject together in a single oral dosage composition, such as a tablet or capsule, or each agent can be administered in separate oral dosage formulations. Where separate dosage formulations are used, an immunosuppressive agent and one or more additional active agents can be administered at essentially the same time (i.e., concurrently), or at separately staggered

times (i.e., sequentially). Combination therapy includes all these regimens.

There can be many advantages to combining two therapeutic agents into one regime. For example, if one combines prednisone and azathioprine, prednisone acts within hours or days whereas aziathioprine can take up to a year bring about an effect. In addition, different therapeutic agents can suppress immune function in different ways which can be necessary for the overall desired immunosuppressive effects. The addition of one treatment agent to another effective regime can also significantly increase the effectiveness of the treatment regime. An example of combination therapy that can be administered to a mammal susceptible to or suffering from narcolepsy to prevent, reduce, arrest, or reverse the development of narcoleptic symptoms comprises administering at least two of the following immunosuppressive agents: an NSAID, a glucocorticoid, hydroxychloroquine, sulfaxalazine, methotrexate, aurothioglucose, aurothiomalate, auronofin, D- penicillamine, azathioprine, cyclophosphamide, cyclosporin A, FK506, or rapamycin.

Another example of combination therapy is treating narcolepsy in a mammal susceptible to or suffering from narcolepsy with a therapeutically effective amount of a glucocorticoid compound used in combination with, for example, a non-steroidal anti-inflammatory compound, hydroxychloroquine, sulfaxalazine, methotrexate, aurothioglucose, aurothiomalate, auronofin; D-penicillamine, azathioprine, cyclophosphamide, cyclosporin A, FK506, or rapamycin. The immunosuppressive agents can also be effectively used in combination with, for example, antibodies to a cytokine or cytokine receptor, an anti-TNF-.A-inverted, antibody, a COX-1 inhibitor, a

COX-2 inhibitor, an iNOS inhibitor, and an antioxidant.

Another regime combines an immunosuppressive agent with at least one of the following active agents: a CNS stimulant and/or an anticataplectic compound (e.g., caffeine, theophiline, theobromine, amphetamine, methylphenidate, dextroamphetamine, methamphetamine, pemoline, mazindol, modafinil, selegiline, ritanserin, viloxazine, CRL 40476, clomipramine, protriptyline, imipramine, desipramine, fluoxetine, paroxitine, sertraline, gammahydroxybutyrate (GHB), clonazepam, carbamazepine, or yohimbine). Other central nervous system stimulants or anticataplectic compounds can include tricyclic or tetracyclic antidepressants, selective serotonin reuptake inhibitors (SSRI) and monoamine oxidase (MAOs) inhibitors."
In col. 14 lines 19-32, Siegel et al. teach "The immunosuppressive agents and other active agents can be formulated with common excipients, diluents or carriers, and compressed into tablets, or formulated as elixirs or solutions for convenient oral administration. The immunosuppressive agents and other active agents can be can also be formulated as sustained release dosage forms and the like.

Administration of the compounds can be achieved in various ways, including oral, buccal, rectal, parenteral, intraperitoneal, intradermal, transdermal, intratracheal, and intramuscular administration. Moreover, the compound can be administered in a local rather than systemic manner, in a depot or sustained release formulation. In addition, the compounds can be administered in a liposome."

Siegel et al. teach, in col. 17 lines 30-52, that "The invention further provides kits comprising an immunosuppressive agent which includes at least one of the following: a

nonsteroidal anti-inflammatory, a glucocorticoid, hydroxychloroquine, sulfaxalazine, methotrexate, aurothioglucose, aurothiomalate, auronofin, D-penicillamine, azathioprine, cyclophosphamide, cyclosporin A, FK506, or rapamycin. Optional additional components of the kit include, for example, other active compounds, in combination with at least one of the following active agents such as, but not limited to, a CNS stimulant and/or an anticataplectic compound (e.g., caffeine, theophiline, theobromine, amphetamine, methylphenidate, dextroamphetamine, methamphetamine, pemoline, mazindol, modafinil, selegiline, ritanserin, viloxazine, CRL 40476, clomipramine, protriptyline, imipramine, desipramine, fluoxetine, paroxitine, sertraline, gammahydroxybutyrate (GHB), clonazepam, carbamazepine, or yohimbine). Other CNS stimulants or anticataplectic compounds can include tricyclic or tetracyclic antidepressants, SSRI and MAO inhibitors. Usually, the kit also contains instructions for carrying out the methods."

It would have been obvious to one of ordinary skill in that art at the time of the invention to have combined a composition comprising an SSRI and a corticosteroid as taught by Siegel. The specific combination of features claimed is disclosed within the broad generic ranges taught by the reference but such "picking and choosing" within several variables does not necessarily give rise to anticipation. *Corninq Glass Works v. Sumitomo Elec.,* 868 F.2d 1251, 1262 (Fed. Circ. 1989). Where, as here, the reference does not provide any motivation to select this specific combination of variables, anticipation cannot be found.

That being said, however, it must be remembered that "[w]hen a patent simply

arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious". *KSR v. Teleflex,* 127 S, Ct. 1727, 1740 (2007)(quoting *Sakraida v. A.G. Pro,* 425 U.S. 273, 282 (1976). "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious", the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." (Ida). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR v. Teleflex*, 127 S, Ct. 1727, 1741 (2007). The Court emphasized that "[a] person of ordinary skill is... a person of ordinary creativity, not an automaton." Id. at 1742.

Consistent with this reasoning, it would have obvious to have selected various combinations of various disclosed ingredients from within a prior art disclosure, to arrive compositions "yielding no more than one would expect from such an arrangement".

Additionally, the dosage amount and sequencing would be obvious to one of ordinary skill in the art where the instantly claimed range is from "low dosage" to "high dosage".

Claims 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Siegel et al. as applied to claims 1-9, 11-12, 15, 19-21, 58, 66, and 73, 74, and 76 above, and further in view of The Merck Index monographs numbers 04972 and 03712.

Seigel et al. is as taught above.

Seigel et al. while teaching the use of anti-inflammatory cytokines, anti-TNFα antibodies, COX-1 inhibitors, COX-2 inhibitors iNOS inhibitors, nNOS inhibitors and antioxidants does not explicitly teach infliximab and/or etanercept etc...

The Merck Index teaches in monograph 04972 that infliximab is a chimeric monoclonal antibody that binds and neutralizes soluble TNFα. It also teaches it has use as an anti-inflammatory.

The Merck Index teaches in monograph 03712 that etanercept is a recombinant protein consisting of the human soluble TNF receptor p75 linked to the Fc portion of human immunoglobulin G1 and that it inhibits the biological effects of TNF. It is taught also to be useful as an anti-inflammatory and an anti-psoriatic.

It would have been obvious to one of ordinary skill at the time of the invention to use etanercept and/or infliximib as the anti-inflammatory cytokines and/or anti-TNFα antibodies of Seigel et al. as etanercept and infliximib are such compounds respectively.

Claims 13-14 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siegel et al. (US Patent No. 6204245B1) as applied to claims 1-9, 11-12, 15, 20-21, 58, 66, and 73, 74, and 76 above, in view of Linden et al. (Psoriasis:

Current perspectives with an Emphasis on Treatment, The American Journal of Medicine, December 1999, vol. 107, pp. 595-605), in view of Guenther (ABSTRACT-Tazarotene combinatin treatments in psoriasis, J. Am. Acad. Dermatol., August 2000, vol. 43, pp. 36-42) and further in view of Mitra (Role of anti-depressant fluoxetine in the puva treatment of psoriasis vulgaris, Indian Journal of Dermatology, Venereology and Leprology, 2001, vol. 67, pp. 292-293).

Seigel et al. is as set forth above.

Seigel does not teach the use of anticholinergic compounds (such as ipratropium or tiotropim), beta receptor agonists (such as ibuterol sulfate, epinephrine, isoproteronol etc...), vitamin D analogs (such as calcipotriene or calcipotriol), psoralens (such as methoxsalen) or retinoids (such as acitretin or tazoretene) in combination with a SSRI and a corticosteroid (or glucocorticosteroid).

Linden et al. teach, in the abstract, that first line treatments for psoriasis include corticosteroids, calcipotriene and tazarotene. Additional treatments include phototherapy with ultraviolet B or photochemistry with psoralens plus ultraviolet A (PUVA), and systemic treatments including methotiexate, acitretin or cyclosporin. On page 599-Table 2, Linden et al. disclose a list of corticosteroids useful in the treatment of psoriasis ranked by potency (the list includes hydrocortisone, dexamethasone, prednisolone, triamcinolone, betamethasone, etc... On page 603, Linden et al. teach that combination therapy wherein agents may be used sequentially or concomitantly with other agents is prudent to prevent side effects.

Guenther teaches, in the abstract, combination regimens comprising tazarotene, calcipotriene, a mid-potency or high-potency steroid, UVB phototherapy and PUVA show enhanced efficacy and tolerability.

Mitra teaches, in the abstract, that the severity of psoriasis vulgaris (psoriasis) is modified by psychological stress. In a trial of ten patients given fluoxetine (to control stress) along with PUVA treatment for psoriasis showed better response and quicker remission than the control group.

The examiner respectfully points out the following from MPEP 2144.06:
"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ....[T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850,205 USPQ 1069, 1072 (CCPA 1980). As all of the compounds have been individually shown to be utilized and effective in the treatment of psoriasis, and as all the references demonstrate combinations of the various compounds in a variety of formulations, the combination of all/or any of the claimed compounds is rendered obvious by the prior art. One would have been motivated to perform such combinations in expectation of achieving better treatments for psoriasis.

Claims 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siegel et al. (US Patent No. 6204245B1) as applied to claims 1-9, 11-12, 15, 19-21, 58, 66, and 73, 74, and 76 above, in view of Ahmed (US Patent No. 6281248) and further

in view of The Merck Manual Section 4-Chapter 44- Asthma.

Siegel et al. is as set forth above.

Siegel et al. does not teach the use of beta receptor agonists (such as ibuterol sulfate, epinephrine, isoproteronol etc...) in combination with a SSRI and a corticosteroid (or glucocorticosteroid).

Ahmed teaches, in the abstract, a method of treating asthma by administration of a composition comprising a selective serotonin reuptake inhibitor (such as sertraline HCl). In col. 1 lines 10-60, Ahmed discloses that sympathomimetic drugs, such as epinephrine, isoproterenol and terbutaline, xanthine drugs and corticosteroid drugs have all been used to treat bronchial asthma.

The Merck Manual teaches, on pages 6-7, that drugs useful in treating/preventing asthma include beta adrenergic agonists such as epinephrine and albuterol and corticosteroids with a combination of a beta adrenergic agent and a corticosteroid giving better results than either individually. Additional drugs useful in the treatment of asthma include thephylline, ipratropium, beclomethasone, budesonide, triamcinolone etc...

The examiner respectfully points out the following from MPEP 2144.06:
"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ....[T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846,

850,205 USPQ 1069, 1072 (CCPA 1980). As all of the compounds have been individually shown to be utilized and effective in the treatment of asthma, and as ail the references demonstrate combinations of the various compounds in a variety of formulations, the combination of all/or any of the claimed compounds is rendered obvious by the prior art. One would have been motivated to perform such combinations in expectation of achieving better treatments for asthma.

Conclusion

Claims 1-21, 58, 66, 73-74 and 76 are not allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAHAR JAVANMARD whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/S. J./

Examiner, Art Unit 1617

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617